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Leiomyosarcoma of the Renal Vein

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The preoperative diagnosis for primary leiomyosarcoma of the renal vein, an extremely rare tumor, is difficult. The tumor predominantly occurs in women and on the left side. Its natural history is toward distant metastases and a poor 5-year survival rate. Nephrectomy and en-bloc surgical resection remain the mainstay of therapy. We present three such cases and review the world literature. © 1996 Wiley-Liss, Inc.

KEY WORDS: **blood vessel, sarcoma, neoplasm, kidney**

INTRODUCTION

Primary leiomyosarcomas of large veins are rare tumors with >50% arising from the inferior vena cava [1]. To date, 25 cases of leiomyosarcoma arising from the renal vein have been reported [2–24]. In this report, we present an additional two cases and provide follow-up information on a third previously reported case from our institution [21].

CASE REPORTS

Case 1

A 70-year-old white male with a history of hypertension and peptic ulcer disease was undergoing radiation therapy for clinical stage C prostate cancer when, 3 weeks into his planned 7-week treatment, he developed radiation enteritis and proctitis with severe diarrhea and associated right lower quadrant pain. Pretreatment pelvic computerized tomography (CT) scan was remarkable only for local prostatic pathology. Abdominal CT scan and magnetic resonance imaging (MRI) showed a 5 × 5 cm mass contiguous with the right renal vein on the medial aspect of the right kidney (Fig. 1). Flow was present in the right renal vein, and there was no evidence of direct caval involvement or obstruction. He underwent a right radical nephrectomy via an 11th rib flank incision in September 1990, with excision of hilar and paracaval lymph nodes.

Gross examination revealed a well-circumscribed 6.4 × 5.0 × 4.2 cm mass arising from an extra renal segment of the renal vein with extension into the perirenal fat at the renal hilum, with a pseudocapsule and no renal parenchymal involvement. Histologic examination disclosed leiomyosarcoma. Immunoperoxidase stains were positive for vimentin and desmin and negative for S-100 protein. Five of five lymph nodes were negative for malignancy. Surgical margins were negative for tumor. One year postoperatively, he was placed on hormonal ablation therapy for his prostate cancer. Follow-up at 51 months reveals no evidence of local, regional, or distal metastatic disease, with a creatinine of 1.0 and a prostate specific antigen of <0.1.

Case 2

A 71-year-old white male with a history of hypothyroidism, gout, and 50 years of smoking a pack per day was noted to have a left renal vein mass on CT scan as part of his abdominal workup in January 1991 for cholelithiasis (Fig. 2). After cholecystectomy, the patient was lost to follow-up and presented in January 1992 with a "lump" on his left chest wall. Excisional biopsy revealed a 3.5 × 2.4 × 2.2 cm mass interpreted as a poorly differentiated leiomyosarcoma, which was most probably metastatic. CT scan showed a 9 × 6 × 6 cm heterogeneous soft tissue mass of the retroperitoneum contiguous with the left renal vein and adjacent to the anterior portion of the mid to lower pole of the left kidney (Fig. 3). In April 1992, he underwent a left radical nephrectomy and paraaortic lymph node resection, via a 10th rib flank incision.

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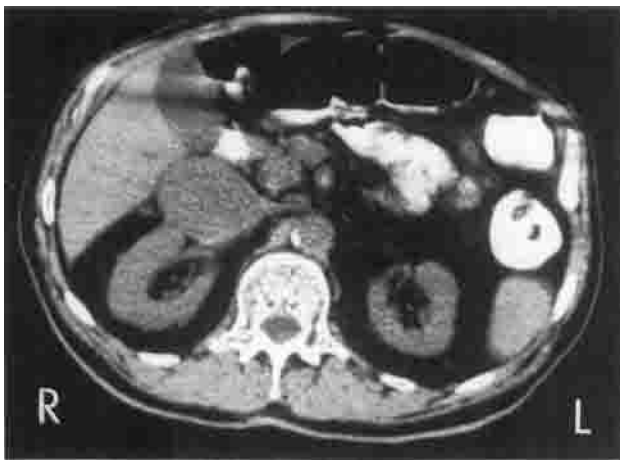

Fig.1. Case 1: Computed tomography of the abdomen showing a 5 cm well-circumscribed mass contiguous with the right renal vein.

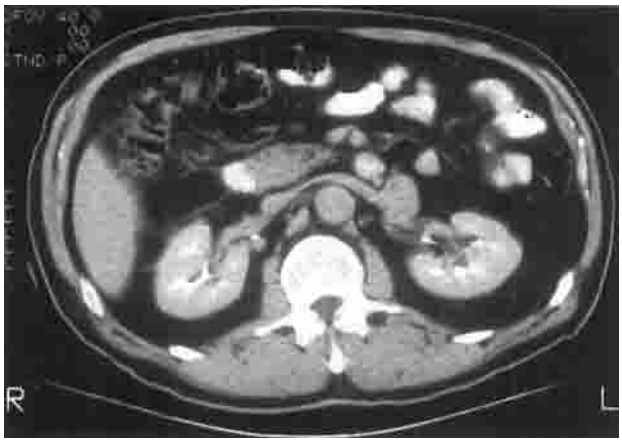

Fig. 2. Case 2: On initial presentation, computed tomography of the abdomen showing a 2 cm mass contiguous with the left renal vein.

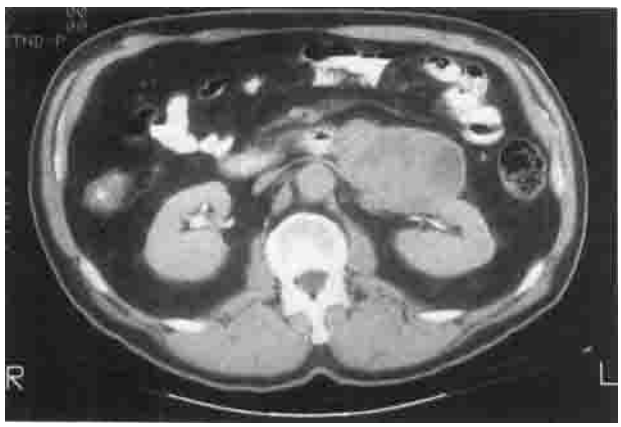

Fig. 3. Case 2: One year later, computed tomography of the same patient, showing continued tumor growth and progression to 10 cm.

Gross examination revealed a 10 × 7.5 × 6.3 cm neoplasm arising from the renal vein, with renal parenchyma, adrenal, ureter, and three of three lymph nodes negative for malignancy. The tumor demonstrated typical fascicles of blunt-ended spindle cells with marked nuclear pleomorphism and was interpreted as a leiomyosarcoma. Immunohistochemical studies were strongly positive for muscle specific actin, focally positive for desmin, and negative for vimentin, factor VIII, S-100, myoglobin, epithelial membrane antigen, and cytokeratin.

In July 1992, he underwent excision of a 2 × 2 cm recurrent metastatic nodule from the left chest wall in the region of the original mass. The following month, he noted a mass in the right calf and underwent excision of a 2 cm metastatic nodule from the right gastrocnemius muscle. He subsequently received local radiotherapy to both anterior chest wall and calf areas. In November 1992, he was noted to have multiple pulmonary metastases on chest CT and was treated with three courses of Adriamycin, ifosfamide, and 2-mercaptoethane sodium sulfonate (Mesna) chemotherapy. In February 1994, 25 months after diagnosis, he died with widespread metastatic disease.

Case 3

A 27-year-old female was initially seen in 1987 complaining of pelvic pain. Ultrasound revealed a 10 cm cystic mass near the tail of the pancreas and the left adrenal gland. The patient refused further treatment at that time. She returned in January 1989, 20 months later, complaining of increasing left upper quadrant pain. A repeat CT scan now showed the same mass enlarged to 15 cm in diameter. A needle biopsy was performed and interpreted as consistent with a low grade sarcoma. A preoperative angiogram revealed a moderately vascular mass in the left retroperitoneum, superior to the kidney with displacement of multiple large blood vessels. The major vascular supply to the mass appeared to be the left adrenal artery.

At laparotomy in June 1989, a 15 cm mass was found superomedial to the left kidney and extending medially over the aorta and completely encasing the left renal vein. In addition, a 1 × 1 cm nodule was found in the left lateral aspect of the liver, which on frozen section was interpreted as consistent with metastatic sarcoma. Hepatic wedge resection, en-bloc tumor resection, and left radical nephrectomy were performed. In addition, she received 1,375 cGy of intraoperative radiation therapy (IORT) to the left renal bed and subsequently an additional 1,375 cGy to a field superomedial to the renal bed, previously occupied by the mass, using standard radiotherapy techniques. Gross examination revealed a grey-tan nodular 15 × 4.0 × 7.5 cm moderately differentiated leiomyosarcoma originating from the left renal vein, with kidney, adrenal, ureter, and renal artery negative for malignancy.

TABLE I. Summary of Reported Cases of Leiomyosarcoma of the Renal Vein

Case	Author	Age/sex	Clinical presentation	IVC[a] Ext.	Side[b]	Treatment[c]	F/U[d] duration and progression	Outcome[e]
1	Varela and Garro [2]	40/F	Abdominal pain and weight loss	No	R	Nephrectomy	96 mo, mets to brain, lung, liver	DOD
2	Bathena and Vasquez [3]	50/F	Abdominal pain and weight loss	No	L	Nephrectomy; lung mets @ 36 mo; tx: Ch (actino-D, N-mus, phenyl)	48 mo	AWD
3	Montgomery et al. [4]	51/F	Abdominal pain weight loss and weakness	No	L	Nephrectomy; Ch (actino-D, phenyl) + XRT(2000R)	36 mo, with pulmonary mets	AWD
4	Gierson and Rowe [5]	54/F	Abdominal mass	No	L	Reaction of tumor (no nephrectomy)	78 mo	NED
5	Appell and Thistlethwaite [6]	60/F	Abdominal pain and weight loss	No	L	Nephrectomy; lung mets @ 4 mo, tx: Ch (dox, dac)	16 mo, with liver + peritoneal mets	DOD
6	Stringer et al. [7]	59/F	Abdominal pain and weight loss	No	L	Resection of tumor (no nephrectomy). Rec locally @ 36 mo; tx: Ch (vin, dact, cyclo, dox) + XRT (4500R)	72 mo	DOD
7	Radhakrishanan et al. [8]	88/F	Epigastric mass	No	L	Nephrectomy; hepatic mets @ 60 mo; tx: resec	90 mo	DNED
8	Kaufman and Gelbard [9]	48/F	Asymptomatic-indicental finding at hysterectomy	Yes	R	Preop XRT (1600R) + Ch (dox), nephrectomy + postop Ch (dox, vin, mtx)	48 mo	NED
9	Herman and Morales [10]	48/F	Flank pain	No	L	Nephrectomy; soft-tissue mets, jaw @ 23, 31 mo tx: resection, lung mets @ 48 mo tx: Ch (dox, dac, cyclo) + resection	48 mo	AWD
10	Dufour et al. [11]	73/F	Abdominal pain, malaise	Yes	R	Tumor resection (no nephrectomy)	18 mo	DOD
11	Hisa et al. [12]	52/F	Abdominal pain and weight loss	No	L	Resection of tumor (no nephrectomy)	8 mo	NED
12	Farges et al. [13]	54/F	Abdominal mass	No	R	Nephrectomy: rec @ 6 mo	6 mo	AWD
13	Martin et al. [14]	54/F	Abdominal pain	Yes	NI	Nephrectomy + Ch	0 mo	A+W
14	Martin et al. [14]	64/M	Abdominal pain	NI	NI	Nephrectomy + Ch; hepatic mets @ 24 mo	24 mo	AWD

TABLE I. Continued

Case	Author	Age/sex	Clinical presentation	IVC[a] Ext.	Side[b]	Treatment[c]	F/U[d] duration and progression	Outcome[e]
15	Vos et al. [15]	65/F	Upper abdominal pain	Yes	R	Nephrectomy, subcut mets @ 24 mo resected	45 mo, mets to lung and bone	DOD
16	Phoa et al. [16]	60/F	Abdominal pain	Yes	R	Nephrectomy with IVC cuff	48 mo, mets to lungs, liver, bones	DOD
17	Farah et al. (17)	40/M	Back pain	No	R	Nephrectomy	NI	NI
18	Martin et al. [18]	48/F	Upper quadrant pain, mass	No	L	Nephrectomy	48 mo	NED
19	Ball and Fisher [19]	58/F	Abdominal pain, weight loss, and mass	No	L	Nephrectomy	12 mo; lung mets	DOD
20	Ball and Fisher [19]	53/F	Abdominal pain, lung mets	No	L	Nephrectomy; Ch @ 4 mo	4 mo; rec in renal fossa, more lung mets	AWD
21	Grignon et al. [20]	61/F	Back pain, hematuria	No	R	Nephrectomy; rec @ 20 mo, partial resec + Ch (dox, dac)	30 mo	DOD
22	Pelton et al. [21]	27/F	Pelvic pain + liver mets	No	L	Nephrectomy liver wedge resec, IORT; Ch @ 9 mo; XRT @ 43 mo	54 mo; Increased mets to liver, scalp, spine + rec in tumor bed	DOD
23	Lakhloufi et al. [22]	60/F	Abdominal pain	No	L	Nephrectomy + jejunal resec	0 mo	A+W
24	Inoue et al. [23]	75/F	Incidental finding	No	L	Nephrectomy	4 mo	NED
25	Lipton et al. [24]	64/F	Abdominal pain + increasing girth	Yes	L	Nephrectomy splenectomy + cavotomy	0 mo	A+W
26	Brandes et al.	79/M	Incidental finding	No	R	Nephrectomy	51 mo	NED
27	Brandes et al.	72/M	Subcut met to chest wall	No	L	Resec subcut met + nephrectomy; @ 5 mo resec chest wall and calf mets; Ch @ 10 mo	25 mo; @ 5 mo calf + chest wall mets; @ 10 mo lung mets	DOD

[a]Inferior vena cava.
[b]R = right; L = left.
[c]mets = metastases; mo = months; tx = treatment; Ch = chemotherapy; actino-D = actinomycin-D; N-mus = nitrogren-mustard; phenyl = phenylalanine; XRT = radiation therapy; dox = doxirubicin; dac = dacarbazine; rec = recurrence; resec = resection; vin = vinblastine; dact = dactinomycin; cyclo = cyclophosphamide; mtx = methotexate; subcut = subcutaneous.
[d]Follow-up.
[e]DOD = dead of disease; AWD = alive with disease; NED = no evidence of disease; DNED = dead and no evidence of disease; A+W = alive and well; NI = no information.

Immunoperoxidase stains were focally strongly positive for desmin and negative for cytokeratin.

In September 1989, she developed a scalp metastasis, and in October 1989, a CT scan revealed a recurrent left retroperitoneal tumor along with multiple liver metastasis. At that time, chemotherapy was recommended; however, the patient refused treatment. In January 1991, the patient agreed to undergo chemotherapy and received four cycles of Adriamycin, ifosfamide, dacarbazine, and Mesna. A repeat CT scan showed continued progression of disease in the liver and left upper quadrant, although she was still relatively asymptomatic. She was subsequently lost to follow-up. By May 1992, she presented with leg weakness and inability to ambulate, secondary to lumbar spinal metastases, which were treated with palliative radiotherapy. In July 1993, 54 months after diagnosis, she died with widespread metastatic disease.

DISCUSSION

Leiomyosarcoma of the renal vein (LMSRV) is extremely rare, with only 25 cases previously reported in the literature [2–24]. Two additional cases along with follow-up of a previously reported case are detailed above. The tumor predominantly occurs in women (23/27 patients or 85%), and over a wide age range of 27–88 years, with a mean of 59 years. The tumor usually also occurs on the left, with 64% (16/25 patients). Presenting symptoms are often vague, and thus diagnosis is often difficult and delayed. The most common symptoms, however, are abdominal pain (17/27 patients or 63%), weight loss (7/27 patients or 26%), and palpable abdominal mass (5/27 patients or 18%). In addition, LMSRV is occasionally asymptomatic (3/27 patients or 11%), being discovered incidentally during treatment or work-up of other diseases. The diagnosis of tumor was incidental in three of these six patients. The retroperitoneal location of these tumors contributes to the clinically occult development of these neoplasms, with patients becoming symptomatic only until after significant tumor progression.

Preoperative diagnosis, as expected with any rare pathological tumor, is difficult. The CT appearance is generally that of a homogeneous, well-circumscribed, solid mass with minimal contrast enhancement in the region of the renal hilum. Magnetic resonance imaging (MRI) demonstrates a well-defined lesion, with isointense signal compared to the kidney on T1-weighted images, and slightly increased signal intensity on T2-weighted images, although less intense compared to the kidney [17,22]. Angiography is also helpful in determining the surgical approach and tumor origin, with noted nonrenal retroperitoneal neovascularity, kidney displacement, and on venous phase, renal vein filling defects, nonvisualization, and/or collateral formation [6,17,21,22,24]. Overall, radiographic studies are often helpful, but not definitive in diagnosing LMSRV. Only after tumor resection and pathologic examination is the diagnosis confirmed. CT guided needle biopsy has been utilized successfully and without significant complications to obtain tissue for diagnostic purposes [16,17,21].

The histologic differential diagnosis of sarcomas arising in association with the renal vein include leiomyosarcoma, angiosarcoma, malignant fibrous histiocytoma, fibrosarcoma, and malignant schwannoma. Ultrastructural and immunohistochemical studies have been helpful in determining tumor origin. Leiomyosarcomas uniformly stain positive for desmin, and occasionally stain positive for smooth muscle actin or vimentin, indicating a smooth muscle cell origin [14,15,19–21,23,24]. Fibrosarcomas are usually vimentin positive and desmin negative, with sharp nuclei and abundant collagen fibers. Hemangioendothelioma are usually factor-VIII positive and vimentin and desmin negative, with atypical, multilayered endothelial cells with round to oval nuclei. Tumors of neuronal origin are S-100-protein positive.

Leiomyosarcomas are typically grey-tan to yellow-white in color, well circumscribed, and whorled in appearance, with occasional areas of necrosis. The tumor commonly encases the renal vein and distorts and/or displaces the renal parenchyma and renal artery without gross infiltration. Microscopically, leiomyosarcomas have a typical pattern of interlacing whorls and bundles of spindle shaped cells, with elongated and blunted nuclei and, less commonly, have pleomorphic, bizarre, irregular, and lobulated nuclei. The number of mitotic figures vary greatly from 2–100 mitoses per 10 high power fields among the reported cases. Electron microscopy typically notes elongated, clefted nuclei, prominent nucleoli, pinocytic vesicles, and intracellular connections [2–25].

Treatment in all 27 cases included surgical resection. The tumor and kidney were removed en-bloc in 23 patients (85%) and local excision of the tumor only was done in four cases (15%). Various regimens of radiotherapy and chemotherapy have been used for metastatic disease. Among them, one patient received preoperative chemotherapy and radiotherapy, another underwent intraoperative radiation therapy and subsequent chemotherapy at recurrence (at our institution), and six patients received chemotherapy at the time of the recurrence, on average >18 months postnephrectomy.

Follow-up data were available for 23 of the patients, ranging from 4 to 96 months (mean 40 months). Ten patients (43%) were dead of disease at 12–96 months (mean 42 months), 6 patients (26%) were alive with disease at 4–48 months (mean 28 months). Of the patients alive with disease, four had metastatic disease, one had a local recurrence in the renal fossa, and one had both local recurrence and metastatic disease. In addition, one patient died of an unrelated, noncancer cause with no evidence of disease at 90 months. Six patients (26%) were alive with no evidence of disease from 4–78 months (mean 39.5 months).

Leiomyosarcoma of the renal vein has a poor 5-year survival rate, with a trend toward distant metastases, rather than regional lymph node involvement or local recurrence. In decreasing frequency, metastases occurred in the lungs (10/16 or 63%), liver (4/16 or 25%), bone (3/16 or 19%), skin and subcutaneous tissue (4/16 or 25%), soft tissue (2/16 or 13%), and brain (1/16 or 6%). Thus the development of an effective adjuvant therapy is clearly needed. To date, nonsurgical therapy, including adjuvant chemotherapy, has been ineffective with LSMRV. Radiotherapy may offer some local control advantage; however, further investigation is needed [26]. The primary therapy for renal vein leiomyosarcoma remains nephrectomy and radical en-bloc surgical resection of the tumor [2–25].

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